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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,981	10/29/2001	Eberhard Hildt	033392-001	7240

21839 7590 11/17/2003

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EXAMINER	
HILL, MYRON G	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 11/17/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/830,981	HILDT ET AL.	
	Examiner	Art Unit	
	Myron G. Hill	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 August 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1- 11* is/are pending in the application.

4a) Of the above claim(s) *3- 11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 October 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I in Paper No. 14 is acknowledged. The traversal is on the ground(s) that all the groups share a common special technical feature and that at least Group II should be rejoined because the DNA of Group II encodes the peptide of Group I. This is not found persuasive because PCT Rule 13.2 holds that unity is lacking when the product is not a contribution over the prior art. The prior art of Wieprecht cited in paper #13 discloses a peptide that meets the limitations of claim 1 and this was not disputed in the traversal. Thus, the invention lacks unity and restriction is proper.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1 and 2 are under consideration in this action.

Claims 3- 11 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Priority

Applicant is requested to update the first line of the specification to indicate that this application is a National Stage Application of PCT/DE99/03506.

Information Disclosure Statement

A signed and initialed copy of IDS, paper#1, is enclosed.

Drawings

The drawings are objected to under 37 CFR 1.83(a) because Figures 3- 5 contain unclear graph lines which will not reproduce well. Additionally, the captions refer to the Figures as having graph lines of certain colors; however, the figures are in black and white and it is unclear which graph lines correspond to which information.

Color photographs and color drawings are acceptable only for examination purposes unless a petition filed under 37 CFR 1.84(a)(2) is granted permitting their use as acceptable drawings. In the event that applicant wishes to use the drawings currently on file as acceptable drawings, a petition must be filed for acceptance of the color photographs or color drawings as acceptable drawings. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and, unless already present, an amendment to include the following language as the first paragraph of the brief description of the drawings section of the specification:

> The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings have been satisfied.

The drawings are also objected to under 37 CFR 1.83(a) because they fail to show SEQ ID#s as described in the specification. Applicant has amended the Brief Descriptions in the specification to include SEQ ID#s but it is not clear which SEQ ID#s go with which sequence.

A proposed drawing correction or corrected drawings are required in reply to this Office Action to avoid **ABANDONMENT** of the application. The objection to the drawings will not be held in abeyance.

Claim Objections

Claim 2 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim.

The amino acid of Figure 1 is from a native HBV surface protein.

A limitation of claim 1 requires that the sequence not be from a native HBV surface protein.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 2 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is not clear in claim 1 how one could know that a sequence is not an HBV sequence without knowing all possible viral sequences. Different subtypes/strains have different sequences as shown in Figure 3, and new subtypes could still be determined. It is not clear what amino acids are specified by the notations i, o, and x. The specification defines the residues on page 3, lines 8- 22. Asparagine and glutamine are listed twice, as hydrophilic and charged side group (used

in x group). Thus, it is not clear if the formula is "XoiioXXioXiX" as written or if it can be interpreted with the "X"s converted to "i"s depending on the amino acid residue and still have the same result. The specification on page 3, lines 1- 4, states that it is not the sequence as such but the order of hydrophobic and hydrophilic residues in an alpha helical motif that are decisive. Asparagine and glutamine can be "i" or "x" and so it is not clear that sequences containing those residues can be assigned to the groups required by the formula in a way to know that peptide will work as claimed. It is also not clear what the metes and bounds of "HBV" is because it seems to include subtypes and related viruses. It is not clear in claim 2 what the metes and bounds of "hybridization" are. The specification on page 5, lines 16- 18, only provides for "common conditions." In claim 2 it is not clear what "latter amino acid" sequence refers to and does this sequence encode the peptide?

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 2 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a motif that enables a peptide to be cell permeable wherein it is not a native HBV surface protein.

The burden of the written description requirement in this application for cell permeability mediating peptide using a peptide of the claimed motif which is not a native HBV surface protein has not been met.

The written description in this case only sets forth sequences of surface proteins of native HBVs. The sequences in the figures are from known HBVs.

Vas-Cath Inc. v. Mahurkar ((CAFC, 1991) 19 USPQ2d 1111), clearly states that "Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See Vas-Cath at page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). It is respectfully submitted that the instant specification, in fact, only shows examples of native HBV surface proteins being used, see Examples 1 and 4 which show HBV and DHBV peptides that have the cell permeability function. However, as defined on page 3, lines 8- 22, proline is not included in the definition of included amino acids. The peptide of Example 1 is excluded from the sequence of the formula shown in claim 1. Also, it is from HBV and thus excluded by the negative limitation. Also, the Figures show several other native HBV surface peptides but nothing that is not a native HBV surface protein. Accordingly, there is evidence that the full scope of the claimed invention was not in Applicant's possession as of the filing date sought.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see Vas-Cath at page 1115).

With the exception of native DHBV surface protein, the skilled artisan cannot envision the encompassed peptides that are not HBV and have this function and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention and a reference to peptides from other native HBV surface proteins are required. See Fiers v. Revel, ((CAFC, 1993) 25 USPQ 2d 1601) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.,((CAFC, 1991) 18 USPQ2d 1016).

Therefore only peptides of native HBV surface proteins, but not the full breadth of the claims as defined by the negative limitation meet the written description provision of 35 USC 112, first paragraph.

Claims 1 and 2 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for DHBV derived cell permeability mediating peptide, does not reasonably provide enablement for peptides that have this function that are not native HBV surface protein derived. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Applicant is reminded that Vas-Cath makes clear that the enablement provision of 35 USC 112 is separate and distinct from its written description provision (see Vas-Cath at page 1115). See also MPEP 2161.

Instant claims are evaluated for scope of enablement based on the Wands analysis. Many of the factors regarding undue experimentation have been summarized in In re Wands, 858 F.2d 731,8 USPQ2d 1400 (Fed.Circ.1988) as follows:

(1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The claims are drawn to a motif that enables a peptide to be cell permeable wherein it is not a native HBV surface protein. The prior art teaches both viral and nonviral derived peptides that are known to have membrane permeability properties, such as *tat*. Structures associated with membrane permeability properties have been noted, see Wiepreht (abstract and first page). As taught in Wiepreht, even though a core structure was used, each substitution had to be tested to determine the change to the property of the peptide. Even knowing a structure/formula for a motif that leads to permeability, Wiepreht had to test each mutation to determine any change in permeability. Applicant only provides examples of other HBV peptides that have similar hydrophobic/hydrophilic assignments in the region of interest (see Figures 3- 5). It is respectfully submitted that the instant specification, in fact, only shows examples of native HBV surface proteins being used, see Examples 1 and 4 which show HBV and

DHBV peptides that have the cell permeability function. However, as defined on page 3, lines 8- 22, proline is not included in the definition of included amino acids. The peptide of Example 1 is excluded from the sequence of the formula shown in claim 1. Also, it is from HBV and thus excluded by the negative limitation. Also, the Figures show several other native HBV surface peptides but nothing that is not a native HBV surface protein. The claims are drawn to "not a native HBV surface protein" and there are no examples of a synthetic non- native HBV surface protein sequence that has the claimed property or the showing of the motif in other known proteins where the function can be correlated to the same property. The claims require anything that is not a native HBV surface protein but there is not a showing that the motif can confer the claimed property to any peptide. Furthermore, the ambiguity of where to assign residues that fall into different groups or where to place residues omitted from the list in the specification, makes it impossible to know what structure the formula requires to have the claimed function or how to interpret a sequence and determine that it does fall within the claimed formula. This will lead to extensive experimentation because many peptides can be interpreted as both comprising the formula and not comprising the formula. The claims are drawn to all peptides of the formula of claim 1 which are not a native HBV surface protein.

Thus, the lack of non-HBV examples and the ambiguity of what defines the formula, there is evidence that the full scope of the claimed invention was not in Applicant's possession as of the filing date sought.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Wieprecht (from IDS).

The claims are drawn to cell permeability peptides that have a formula as recited in claim 1 and that are not native HBV surface proteins.

Wieprecht discloses a peptide that has cell permeability functions and has a sequence that fits formula I (see Table 1, peptide 180° M2a, GIGKF LH**KVG SFIKS WKE**I MNS converts to "XoiioXXioXiX" as defined in claim 1.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Myron G. Hill whose telephone number is 703-308-4521. The examiner can normally be reached on 9am-6pm Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Myron G. Hill
Patent Examiner
November 12, 2003

JEFFREY STUCKER
PRIMARY EXAMINER